

REMARKS

This paper is a response to the outstanding office action of December 11, 2008. Claims 1-3, 6-7 and 89-102 are pending in the present application. Claim 93 is amended to address the Examiner's objection to that claim. Claims 94-102 are newly added to provide further dependent claims reflective of the restricted invention. In claim 1, Applicants previously amended the term *comprising* which is an open term to the term *consisting essentially of*, a term which is more limited in scope. The term *consisting essentially of* is used to describe crosslinked diblock polymers according to the present invention which contain diblock (AB) polymers which are crosslinked and avoid substantial quantities of multiblock polymers within the polymer backbone which is crosslinked. Moreover, the compositions which are claimed clearly distinguish over nanoparticles (Spenlehauer) and multiblock polymers (Domb) of the prior art, either alone or in combination. Claims 4-5 and 8-88 were previously canceled without prejudice as was all previously canceled subject matter. It is respectfully submitted that the amended claims as presented herein meet the requirements of 35 U.S.C. and are clearly patentable over the art of record.

A review of the present claims in comparison to the disclosures cited against the instant application evidences that the presently claimed compositions are patentable over the disclosures of Spenlehauer, et al., US Patent no. 5,6834,723 (Spenlehauer), in view of Domb, et al., US Patent no. 5,578,723 ("Domb"). Indeed, a fair reading of those disclosures suggests that a combination of those references actually *teaches away* from the presently claimed invention.

The Examiner has objected to or rejected previously pending claims 1-3, 6, 7 and 89-93 under 35 U.S.C. §103 as being invalid over Spenlehauer, in view of Domb for reasons which have been articulated in the September 11, 2008 office action. Applicants shall address these issues separately in the sections which follow.

The Objection to Previously Pending Claim 93

The Examiner has rejected previously pending claim 93 as being of improper dependent form. In response, Applicants have amended claim 93 to be dependent on claim 2, rather than claim 92. It is respectfully submitted that the amendment to claim 93 obviates the Examiner's objection.

The Rejection of Claims 1-3, 6-7 and 89-93 as being Obvious Over Spenlehauer, in view of Domb

The Examiner has rejected claims 1-3, 6-7 and 89-93 under 35 U.S.C. §103(a) as being unpatentable over the disclosure of Spenlehauer, in view of Domb for the reasons which are set forth in detail on pages 5-6. It the Examiner's view that Spenlehauer teaches nanoparticles based upon polyoxyethylene and polylactic acid block copolymers, wherein one end of the polymer is end-capped with an alkyl group. Domb is cited for teaching nanoparticles of non-linear hydrophilic-hydrophobic multiblock copolymers, which polymers may include polylactic acid and polyethylene glycol and be used as described in the office action on page 6, top. From this combination of disclosures the Examiner argues that it would been obvious to combine the teachings of Spenlehayer and Domb and cross-link the polymers with gamma-emitting moieties or biologically active molecules. From this description the Examiner concludes that the present invention is *prima facie* obvious over the cited prior art. Applicants respectfully traverse the Examiner's rejection of the pending claims.

The present invention is directed to novel crosslinked diblock polymers *consisting essentially of* AB diblocks which are crosslinked, where A is a polyester block and B is a polyether (poly)oxyalkylene block which is end-capped with a non-reactive group. By using the

term *consisting essentially of* as that term is given its ordinary meaning, compositions according to the present invention provide AB diblock polymeric compositions which are crosslinked. As claimed, the present invention clearly distinguishes over the compositions of Spenlehauer inasmuch as Spenlehauer *avoids crosslinking* in order to limit the size of the polymeric compositions so that they will be useful as nanoparticles. The Spenlehauer particles have a particular molecule weight and are not crosslinked. The chemical composition of Spenlehauer is designed to be delivered through the capillaries of a patient and avoid the reticuloendothelial system within a cell. In contrast, the polymeric compositions according to the present invention exhibit unexpected activity as storage stable compositions of *definitive* structure, the size or molecular weight of which can be fairly easily controlled, modified and used in a number of applications, e.g., to prevent or reduce the likelihood of adhesion formation subsequent to medical procedures such as surgery, for producing surgical articles including stents and grafts, as coatings, sealants, lubricants, as transient barriers in the body, for materials which control the release of bioactive agents in the body, for wound and burn dressings and producing biodegradable objects. Thus, the presently claimed compositions rely on the nature of the crosslinked AB diblock systems which are amenable to significant compositional and molecular weight flexibility and may be modified consistent with this flexible approach to significantly change the physicochemical properties of the claimed polymer composition. This may be done *within a diblock AB copolymer, by modifying the length of the A block and/or the B block, through the use of different types and amounts of crosslinking agents or through combinations of all of these approaches*. Thus, by virtue of the chemical compositions which are presently claimed, a significant degree of flexibility may be incorporated into the polymeric composition. The same cannot be said of the prior art. The definitive, yet flexible structure of the polymeric compositions of the present invention clearly distinguishes over the art taught polymeric compositions. The present compositions may be directed to vary greatly in viscosity and in form with contemplated compositions being used primarily as viscous solutions and gels, although numerous other forms are clearly contemplated by the present invention.

The compositions of the present invention, because they are based upon diblocks which are end-capped, generally have molecular weights which are significantly reduced in comparison to triblock/multiblocks, for example, those which are disclosed in Cohn, but which may be modified to provide substantial structure which is distinguishable from the prior art compositions. The advantage of the present polymers is that they can be used to produce biodegradable or bioerodible viscous formulations, films or structures which exhibit varying viscosities for purposes of providing unique polymers, in particular, post-surgical polymers which can be delivered to a site within a patient's body to prevent adhesion formation. This can be done despite the crosslinked structure of exemplary polymers of the present invention. It is the combination of stability as well as the ability to readily control viscosity of the polymeric materials (at low or high viscosities, as defined by the length of the A or B block and the amount of crosslinking which occurs) which makes these polymers patentably distinguishable over the polymers disclosed by Spenlehauer, in view of Domb. Compositions according to the present invention are particularly attractive for use in medical applications, and in particular, as barriers for preventing or reducing adhesion and in delivering drugs and other bioactives to patients. The relatively low viscosity, yet with high structural integrity reflective of a crosslinked composition in certain applications, gives advantageous structural features which enable polymers according to the present invention to be delivered in applications where films are contraindicated and where nanoparticles, such as are taught by the prior art cannot provide sufficient structural integrity and size. Numerous other uses for the present compositions are also contemplated by the invention.

An important feature of the present invention is that the various and flexible physicochemical characteristics of the polymeric material can be readily controlled through the use of crosslinked AB diblocks as claimed. The same cannot be said of the prior art teachings which has chemistry which is not controlled with the same degree of accuracy and stability as the present invention.

As discussed, it is respectfully submitted that Spenlehauer does not disclose or suggest the presently claimed compositions because Spenlehauer is directed to uncrosslinked copolymers which are in the form of nanoparticles which are specifically designed to be delivered through the capillaries of a patient without being impacted by the reticuloendothelial system. To do this, Spenlehauer *avoids* the use of crosslinkers because such an approach would substantially increase the size of the polymeric compositions and detract from the utility of the compositions for which the Spenlehauer invention was directed. The present invention is actually incompatible with the requirements of Spenlehauer, namely the delivery of compositions to the patient through the capillaries of the patient which *evade* the reticuloendothelial system. In the present invention, the compositions are not designed to flow freely through capillaries, but rather are injected into a site to prevent adhesions or to deliver a drug.

Domb, also cited against the present invention, does nothing to cure the deficiencies of Spenlehauer in failing to disclose or suggest the present invention. Domb is directed to multiblock copolymers which are crosslinked to produce nanoparticles and microparticles of *non-linear* multiblock polymers. In Domb, a hydrophilic block polymer and a hydrophobic block polymer are each separately bound to a crosslinker (which may contain multiple functional groups) to produce nanoparticle or microparticle spheres which are designed to be delivered through the bloodstream of a patient. The polymers of Domb are synthesized to provide particles which have polyalkylene oxide polymers on the surface of the polymeric particles. The particles are said to have a prolonged half-life in the blood. By virtue of the specific chemistry disclosed in Domb which relies on the use of hydrophilic and hydrophobic copolymers which are separately bonded to the crosslinking agent, *but not to each other*, the Domb polymeric compositions obtain a particular chemical structure in solution, with the inner portion of the particle being made up of hydrophobic polymer and the outer portion being made from polyoxyalkylene. This particular structure of Domb is said to provide greater half-life in the blood for delivery of bioactive agents which may be affixed thereto. Domb neither disclosed nor

even remotely suggests the present invention, which requires an AB diblock, wherein the polyoxyalkylene polymeric chain is directly bonded to the polyester chain. Domb is silent on compositions such as those of the present invention because Domb provides a chemistry which produces an oriented chemistry which provides an internal spherical hydrophobic region and an outer region which is composed of polyoxyalkylene groups. This orientation is critical to Domb which teaches that the three-dimensional structure in solution (the blood) influences delivery of the nanoparticle in the bloodstream of the patient.

One of ordinary skill in the art, relying on the teachings of Spenlehauer and Domb would not produce the compositions of the present invention, because that person of ordinary skill would recognize that a crosslinked polymer utilizing the Spenlehauer polymers (which according to those teachings are *purposely* neither crosslinked nor chain-extended), would risk the favorable biological properties which the Spenlehauer polymers were designed to address. Indeed, one of ordinary skill would *avoid* crosslinking the Spenlehauer polymers because to do so would be to negate and work against the very teachings of that reference and the favorable biological characteristics those polymers obtained *as a consequence* of avoiding chain-extension and crosslinking. Polymeric materials which are crosslinked are of higher molecular weight and more complex three dimensional chemical structures and work in *complete contravention* to the Spenlehauer teachings. Thus, Spenlehauer clearly *teaches away* from the present invention. Domb, as described, relies on a completely different chemical structure wherein the two physicochemically distinguishable polymeric chains are separated from each other by a linker- clearly to provide flexibility to the overall three dimensional polymeric structure provided- again to instill certain biological characteristics which relate to the delivery of polymer within the capillaries of the patient and the avoidance of certain immune reactions in the patient. But Domb and Spenlehauer both purposely avoid the type of chemistry of the present invention- because such chemistry is otherwise incompatible with the teachings of those references.

It is respectfully submitted that there can be no more cogent an argument for the non-obviousness of an invention where, as here, the prior art cited against the invention teaches that the presently claimed compositions should not be made because the invention *contravenes* the rationale for the chemistry in the cited prior art. This is precisely why the presently claimed compositions are patentable over Spenlehauer in view of Domb and why a combination of those references does not in any way negative the present invention. If anything, the teachings of the prior art fully support the patentability of the present invention.

Consequently, for the reasons which are presented hereinabove, it is respectfully submitted that the claimed invention is in compliance with the requirements of 35 U.S.C. Applicants respectfully assert that the claims set forth in the amendment to the application of the present invention are now in condition for allowance and such action is earnestly solicited.

Applicants have added 9 claims, making the total number of claims in the present application 19 (one independent). No fee is due for the presentation of this amendment. Small entity status pertains to this application. A petition for an extension of time is enclosed as is the fee. The Commissioner is authorized to charge any deficiency in fee or to credit any overpayment to deposit account 04-0838.

Respectfully submitted,

COLEMAN SUDOL SAPONE, P.C.

By: 

Henry D. Coleman

Reg. No. 32,559

714 Colorado Avenue

Bridgeport, Connecticut 06605

(203) 366-3560

Dated: February 11, 2009

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Henry D. Coleman (Reg. No. 32,559)